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Uterine Artery Doppler and Prediction of Preeclampsia

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Abstract

The purpose of this study was to determine the accuracy of screening for pregnancy hypertension disorders using maternal serum biomarkers and uterine artery Doppler during the first trimester. At 11-13 weeks, uterine artery Doppler and serum measurements were taken from prospectively enrolled nulliparous women. In this study, maternal features, uterine artery Doppler imaging, and serum placental biomarkers (pregnancy-associated plasma protein-A, Inhibin-A, placental protein, A disintegrin and metalloprotease, free B-hCG, placental growth factor) were all collected and evaluated. Twenty women (2.2 percent) experienced prenatal hypertension, and forty women (4.5 percent) developed preeclampsia, with nine (1.0 percent) developing early-onset preeclampsia and sixteen (1.8 percent) developing severe preeclampsia, according to the findings.

A combination screening model that included clinical features, pregnancy-associated plasma protein-A, Inhibin-A, and placental growth factor was found to be effective in detecting 75 percent of early-onset preeclampsia with a false-positive rate of 10 percent. Uterine artery Doppler, placental protein, A disintegrin and metalloprotease were all found to have no effect on diagnosis accuracy after adjusting for clinical factors. When combined with first-trimester maternal serum biomarkers (pregnancy-associated plasma protein-A, Inhibin-A, and placental growth factor), a combination of clinical features and placental growth factor can give an accurate screening for early-onset preeclampsia in nulliparous women.

***Keywords*— uterine artery Doppler, preeclampsia, screening, Erbil, Kurdistan Region of Iraq.**

I. INTRODUCTION

Preeclampsia causes around 2 percent to 5 percent of all pregnancies, however it is a difficult disease to anticipate and treat because of its unpredictable nature (Tianthong & Phupong, 2021). Preeclampsia is an intriguing target for researchers looking to develop a reliable screening test since it affects so many pregnant women (Oancea et al. 2020). If we could identify people who are at risk, we could strengthen their prenatal surveillance and, as a result, reduce the intrinsic maternal and fetal morbidity and mortality that are linked with severe preeclampsia and eclampsia, as well as the associated maternal and fetal mortality (Prakansamut & Phupong, 2019).

Preeclampsia is a disorder that affects around 3 percent of pregnant women globally and is responsible for a significant amount of maternal and fetal morbidity and mortality (Yu et al. 2017). Estimating each woman's unique risk would allow for more appropriate antenatal surveillance, as well as the testing of preventive treatments such as low-dose aspirin in high-risk groups that were previously identified (Cui et al. 2017). However, it is expected that the use of prophylactic treatments will be more effective if they are initiated earlier in pregnancy, preferably before 16 weeks. The development of a reliable mechanism for the early identification of high-risk populations would be critical in this regard. Women who are at risk are currently recognized primarily based on their clinical history. When it comes to developing preeclampsia, nulliparity is considered to be one of the most significant clinical risk factors (Soongsatitanon & Phupong, 2020). A higher body mass index, as well as other medical disorders such as prepregnancy diabetes, prior preeclampsia, or chronic hypertension, are also considered important. However, screening for preeclampsia based solely on maternal history will only uncover 30% of women who may develop preeclampsia in the future(Pedroso et al. 2018). The clinical risk-based technique is ineffective in the case of nulliparous women

who do not have any additional risk factors. When maternal serum indicators and uterine artery Doppler (uAD) are combined, it may be possible to increase the accuracy of illness prediction in this population. PAPP-A, placental protein (PP), Inhibin-A, placental growth factor, and A disintegrin and metalloprotease have all been proposed as blood markers for preeclampsia screening during the first trimester of pregnancy (Rashid et al. 2020). Although uAD screening has primarily been examined in the second trimester of pregnancy, Doppler ultrasound in the first trimester of pregnancy has lately showed some promise. 18-20 According to the findings of a systematic review of screening tests for preeclampsia, no single test is currently available that has a high degree of diagnostic accuracy. A combination screening approach including a number of relevant markers is more likely to yield the most accurate results. Preventive screening during the first trimester would have significant advantages over screening during the second trimester since it would allow for more timely and effective treatment options (Salem & Ammar, 2018). We wanted to look at the diagnostic accuracy of various key biomarkers for the diagnosis of subsequent preeclampsia in the first trimester of pregnancy in a group of nulliparous women, and how they were related to maternal features and uAD (Litwińska et al. 2017).

According to the literature, preeclampsia is characterized as high blood pressure (>140/90) with proteinuria (>300mgina24hspecimen) after 20 weeks of pregnancy (Okwudire et al. 2019). The condition is further split into mild and severe variants, with HELLP syndrome (hemolysis, increased liver function tests, and low platelets) occurring at various points throughout the spectrum of the disease's progression. Preeclampsia is recognized to have its origins in faulty placentation and insufficient trophoblastic invasion of the spiral arteries, which are the main blood vessels of the body (Allen & Aquilina, 2018). Normally, throughout pregnancy, the spiral arteries undergo remodeling, transitioning from a high resistance vascular bed to a low resistance vascular bed over the length of the pregnancy. In individuals who eventually develop preeclampsia, we know that this does not occur in the usual course of events because of histologic examination(Razavi et al. 2019).

However, despite the fact that research continues to find vasoactive mediators and characteristics that may be causal or predictive of preeclampsia, we still lack the ability to detect at-risk patients and perhaps treat them before the condition manifests itself. It is possible that the use of uterine artery Doppler waveform interrogation at various time periods during pregnancy, in conjunction with or without biomarkers, will provide the best possibility for early identification. Researchers have attempted to identify at-risk patients by looking for indicators of injury or dysfunction in the many organ systems that have been implicated in the disease (Ratiu et al. 2019). These procedures have ranged from serum tests and the Roll-over Test to Angiotensin II infusions to identify patients who are at risk of developing hypertension. Despite the fact that several first appeared promising, subsequent study has revealed that there is no screening test that meets the characteristics of being inexpensive, simple to do, and sensitive, as well as having a therapy for it. Other prerequisites to early detection of preeclampsia include the necessity for a screening that occurs before the first wave of placental angiogenesis/branching, which allows any preventative methods to be tested and implemented when they are most likely to be beneficial (Tianthong & Phupong, 2021).

The introduction of pulsed wave Doppler ultrasound techniques has resulted in improvements in a number of areas of obstetrics and holds out the prospect of the development of a screening test for preeclampsia in the future. Testing has been carried out at various periods of pregnancy, and for the sake of this review, the studies have been split by trimester. Finally, we will examine the use of aspirin for illness prevention in the absence of other disorders (for example, antiphospholipid syndrome), which would otherwise necessitate the administration of heparin and/or aspirin to treat the disease (Oancea et al. 2020).

First, the transducer is inserted into the patient's inguinal canal and moved along the uterine artery to obtain a pulsed wave Doppler flow velocity waveform of the uterine artery. After that, two-dimensional ultrasound imaging with color Doppler is used to detect the iliac and uterine vessels just lateral to the uterus, which are then removed. By putting the transducer in the inguinal canal and identifying the external iliac vessels, the uterine artery Doppler can be acquired using color Doppler, as shown in Figure 1A. The uterine artery can be seen crossing these veins at a nearly 90-degree angle, indicating that it is present. When compared to the iliac vessels, the uterine vessel can be sampled from either the distal or proximal region of the vessel, depending on the situation. When the angle of insonation between the Doppler waveform and the vessel is kept as near to 0 degree as possible, it is possible to obtain the optimal flow velocity waveform profile. This requirement for minimizing the angle of insonation to less than 30 degrees is only necessary when determining a genuine volume flow (for example, mL/min). The absolute value of the blood's velocity (for example, cm/s) must be included in the computation in order to determine flow volumes. Resistance indices, on

the other hand, are determined by comparing relative values rather than absolute values (systolic to diastolic ratio, resistance index, and pulsatiliity index), hence the angle of insonation is not crucial for the measurements (Prakansamut & Phupong, 2019).

II. METHODS

In this prospective cohort study, we enrolled 1000 pregnant women, at the time of Down syndrome screening at 11-13 weeks, when they were screened for Down syndrome. All pregnant women who were multiparous or who had multiple births were removed from the study, as were pregnancies with a severe fetal chromosomal or structural abnormalities. Before participating in the study, all women were required to provide written informed permission, and the experiment was authorized by the university's institutional ethics committee. In order to be included in the study, women had an interview with a research nurse and completed a standardized questionnaire that included questions about maternal age, ethnic origin, smoking during pregnancy, and medical issues. The body mass index (BMI) of the mother was computed after her weight and height were measured. An ultrasound examination was performed to diagnose significant fetal anomalies, measure nuchal translucency thickness, and assess the length of the crown-rump region, which was used to determine the gestational age. At the same visit, both uterine arteries were investigated by transabdominal Doppler velocimetry, which was performed by trained sonographers using a standardized technique and utilizing the same equipment. 22 Color flow mapping was used to identify each uterine artery, which was located at the level of the apparent crossover with the external iliac vessels. This method was chosen because it is very comparable to the well-validated second-trimester strategy for uAD, which was utilized previously. The use of pulsed-wave Doppler to cover the entire breadth of the vessel was accomplished after it was determined that the angle of insonation was less than 50 degrees. The signal was refreshed until at least six clear, similar consecutive waveforms could be produced by analyzing the data. The pulsatility index (PI) was measured from both uterine arteries, and the mean, lowest, and maximum PIs from both sides, as well as the presence of a protodiastolic notch, were all recorded and plotted together. As previously explained, it was hypothesized that the lowest PI would more accurately reflect placental function than the mean PI. They weren't transmitted to the doctors in charge of the follow-up and they weren't recorded in the ultrasound report from the first trimester. A total of four aliquots of maternal nonfasting blood samples were obtained and promptly centrifuged at 4000 rpm for 10 minutes, after which they were split and stored at 80o C until needed for the analyses. A completely automated solid-phase enzyme-labeled chemiluminescent immunometric assay and a solid-phase 2-site chemiluminescent immunometric assay were performed on the IMMULITE 2000, respectively, to quantify free B-hCG and PAPP-A levels (Siemens Medical Solutions Diagnostics, Los Angeles, CA). In PAPP-A, the total coefficients of variation (CV) were 3.8 percent and 6.0 percent at 0.4 and 4.2 IU/L, respectively; in free B-hCG, the total coefficients of variation (CV) were 4.5 percent and 4.8 percent at 10 g/L and 312 g/L, respectively. The presence of inhibin-A was determined using an automated 2-site chemiluminescent immunometric assay using the Access-2 system (Beckman-Coulter, Chaska, MN). At 51 ng/L and 331 ng/L, the total imprecisions were 5.9 percent and 4.9 percent, respectively, according to the results. The concentrations of PP, PlGF, and ADAM12 in maternal serum were determined using DELFIA kits (AutoDELFIA PP RUO 4062-0010, DELFIA Xpress PlGF 6007-0010, and AutoDELFIA ADAM12 RUO 4025-0010, respectively) obtained from Perkin-Elmer Life and Analytical Sciences (Perkin-Elmer Life and Analytical Sciences). Each of the assays had a total variance of 6.6 percent, 4.8 percent, and 4.3 percent in total, respectively. It was only possible to assess PlGF in 531 women since the test was not initially scheduled and because additional serum was not available for women who were included in the trial during the first year. The laboratory professionals who performed the biochemical assays were not aware of the subjects' clinical status, and the results were not disclosed to the clinicians, with the exception of the first-trimester free B-hCG and PAPP-A levels, which are routinely reported for Down syndrome screening in the United States. The information on pregnancy outcomes was gathered from the hospital's medical records. During the study, the records of all women with hypertension were examined by two independent investigators who were not aware of the findings of the first-trimester test to decide if the final diagnosis was chronic hypertension, preeclampsia, or gestational hypertension. In order to provide quality control, we reviewed the records of 50 randomly selected women who did not have any hypertensive disorders during their pregnancy. The International Society for the Study of Hypertension in Pregnancy provided the definitions of preeclampsia and gestational hypertension, which were used in this study. Resting blood pressure greater than 140/90 mm Hg on two occasions at least 4 hours apart, as well as proteinuria greater than 0.3 g/d at 20 weeks in previously normotensive women, were considered to be signs of preeclampsia. Gestational hypertension was described as high blood pressure during pregnancy without the

presence of proteinuria. In this study, preeclampsia detected before 34 weeks was considered early-onset preeclampsia. As previously described, severe preeclampsia was defined as having a blood pressure of 160/110 mm Hg, proteinuria of 5 g/d, or the presence of an adverse condition, which could be anything from maternal symptoms to maternal signs of end-organ dysfunction to abnormal maternal laboratory testing to fetal compromise, among other things.

III. FINDINGS

Number of women who were consecutively enrolled, 107 (10.7 percent) were excluded from further analysis due to multiparity (n 48), gestational age outside the inclusion criteria (n 39), twin pregnancy (n 2), major fetal defect (n 2), miscarriage or fetal death before 20 weeks (n 6), or missing outcome data. Multiparity was defined as the presence of two or more children in the same pregnancy (n 10). Thirty-nine percent of the remaining 893 women had gestational hypertension (2.2 percent), and forty percent developed preeclampsia (4.5 percent), including nine cases of early-onset preeclampsia (1.0 percent) and 31 cases of late-onset preeclampsia (0.1 percent) (3.5 percent).

Table 1- First-trimester biomarkers

Factors	Unaffected	GH	PE	Severe PE	Early- onset PE
ADAM12	593.00 (467.74–759.00)	529.00[a] (385.00–705.04)	545.84 (347.01–726.47)	577.99 (429.25–726.00)	637.88 (481.59–850.20)
PlGF	27.57 (21.23–35.56)	29.98 (18.74–36.24)	23.71 (19.01–33.72)	27.81[a] (17.32–36.28)	27.81 (15.77–35.99)
PP	77.25 (58.79–104.80)	63.00[a] (50.14–84.58)	70.73 (51.02–95.23)	70.36 (48.77–97.83)	70.02 (49.00–84.42)
PAPP-A	2.44 (1.54–3.77)	1.52[a] (1.09–2.48)	1.78[a] (1.13–3.49)	1.77[a] (1.00–3.05)	2.76 (1.59–2.94)
Inhibine-A	250.60 (184.50–350.60)	226.90 (163.75–328.35)	254.20 (193.70–346.60)	254.20 (207.95–381.85)	361.90 (218.40–665.20)

P Value=0.05 (*t* test, compared with unaffected group).

Several of pregrnant women were diagnosed with severe preeclampsia (1.8 percent). Table 1 is a summary of the traits that distinguish women. Preeclampsia or gestational hypertension were found in a similar proportion of women to those who were not afflicted, regardless of maternal age or smoking status. Women with preeclampsia or gestational hypertension had significantly higher BMIs at the time of enrolment than women who were not afflicted. Early-onset preeclampsia was more common in Afro-Caribbean women and in women who had a preexisting medical condition, according to the study (P .05). In the unaffected group, all biomarkers (with the exception of PP) were shown to be substantially linked with gestational age and BMI (except PlGF). There was no correlation found between mother age and any of the outcomes. Women of AfroCaribbean descent had significantly higher PlGF (1.39 vs 1.00; P.001), ADAM12 (1.21 vs 0.98; P.0012), and PAPP-A (1.37 vs 0.97; P.001) levels compared to those of non-African descent. PlGF (1.25 versus 0.98; P.015), ADAM12 (0.81 vs 1.01; P.001), PAPP-A (0.87) and free B -hCG (0.87 versus 1.02; P.001), and free B -hCG were also found to be significantly different between smokers and nonsmokers (0.78 vs 1.01; P .002).

Table 2- Uterine artery Doppler

Findings	Lowest (PI Value)	Medium (PI Value)	Highest (PI Value)
GH	1.14 (0.85–1.90)	1.28 (1.08–2.16)	1.27–2.24
Late PE	1.10 (0.79–1.49)	1.57 (1.21–1.78)	1.92 (1.47–2.24)
Early -Onset PE	1.48 (0.55–1.74)	1.58 (0.82–1.78)	1.65 (1.11–1.92)

Severe PE	1.48 (0.63–1.91)	1.59 (0.83–1.98)	1.81 (1.04–2.06)
PE	1.13 (0.73–1.55)	1.57 (1.18–1.76)	1.81 (1.39–2.19)
Unaffected	1.06 (0.79-1.48)	1.40 (0.82-1.78)	1.69 (1.22-2.18)

The levels of biomarkers are shown in Table 2 in relation to the outcome of the pregnancy. Inhibin-A levels were significantly greater in women who had severe preeclampsia (median MoM, 0.77) and PlGF (median MoM, 0.62), compared to women who did not develop severe preeclampsia (median MoM, 1.67). No statistically significant differences were found in the MoMs of free B-hCG, PP, and ADAM1.

Table 3- Biomarkers and uterine artery Doppler

Factors	**Preeclampsia**	**Severe preeclampsia**	**Early-onset preeclampsia**
L-PI	0.515 (0.413–0.618)	0.601 (0.445–0.757)	0.529 (0.275–0.784)
M-PI	0.553 (0.462–0.643)	0.584 (0.440–0.728)	0.482 (0.271–0.694)
PP	0.517 (0.427–0.608)	0.514 (0.391–0.638)	0.483 (0.271–0.695)
Inhibin-A	0.546 (0.450–0.642)	0.569 (0.434–0.704)	0.708 (0.495–0.922)
Free *B*-hCG	0.548 (0.453–0.643)	0.560 (0.425–0.696)	0.510 (0.285–0.736)
PlGF	0.654 (0.521–0.787)	0.711 (0.541–0.882)	0.747 (0.509–0.984)
ADAM12	0.500 (0.411–0.589)	0.531 (0.414–0.648)	0.420 (0.235–0.604)
PAPP-A	0.570 (0.482–0.657)	0.661 (0.556-0.766)	0.622 (0.476-0.767)

The findings of uAD are shown in Table 3. Log PI was found to be independently predicted by fetal CRL in the unaffected group, but not by ethnic origin, maternal BMI or age in the affected group, according to a linear regression analysis. In the first trimester, there were no statistically significant differences between patients and controls in the lowest, mean, and highest uAD PI MoMs.

Table 4- Integration of maternal characteristics

Elements	**Preeclampsia**	**Severe preeclampsia**	**Early-onset preeclampsia**
PlGF, Inhibin-A, PAPP-A, L-PI	0.815 (0.737–0.893)	0.890 (0.803–0.977)	0.994 (0.982–1.000)
Inhibin, PAPP-A, L-PI	0.745 (0.660–0.829)	0.814 (0.712–0.916)	0.834 (0.683–0.986)
PlGF, Inhibin-A, PAPP-A	0.793 (0.714–0.873)	0.851 (0.749–0.953)	0.969 (0.910–1.000)
PAPP-A, Inhibin A	0.742 (0.660–0.824)	0.809 (0.715–0.904)	0.851 (0.714–0.989)
PlGF, Inhibin A	0.794 (0.713–0.876)	0.815 (0.690–0.941)	0.958 (0.877–1.000)
PlGF, PAPP-A	0.795 (0.710–0.880)	0.814 (0.695–0.933)	0.844 (0.584–1.000)
Inhibin-A	0.754 (0.677–0.830)	0.793 (0.702–0.883)	0.841 (0.703–0.980)
PAPP-A	0.742 (0.658–0.827)	0.797 (0.702–0.892)	0.780 (0.624–0.937)
PlGF	0.790 (0.702–0.878)	0.786 (0.645–0.926)	0.847 (0.593–1.000)

The incidence of bilateral notching was likewise similar between the groups. As indicated in Table 4, the AUC for all biomarkers and Doppler results is calculated. PlGF, Inhibin-A, and PAPP-A were found to be the most accurate predictors of early-onset preeclampsia (AUC of 0.75, 0.71, and 0.62).

IV. DISCUSSION

The findings of this prospective study in nulliparous women have confirmed some of the findings of previous studies, namely that low levels of maternal serum PAPP-A and PlGF in the first trimester, as well as increased levels of serum InhibinA, are associated with an increased risk for the development of preeclampsia in the second trimester of pregnancy. Women who develop early or severe preeclampsia, as opposed to those who develop late or mild preeclampsia, have higher levels of the hormone. We also confirmed that women with a higher body mass index (BMI) and women of Afro-Caribbean race are at greater risk of developing hypertensive problems while pregnant. We were unable to validate the predictive accuracy of other possibilities, such as PP, ADAM, and free B hCG, due to a lack of sufficient data. Aside from finding a link between aberrant first-trimester uAD and subsequent preeclampsia, we discovered that adding Doppler to the screening process, whether alone or in combination with PAPP-A, PlGF, and Inhibin-A, did not increase the diagnostic accuracy of the screening process. The prospective design of this study, which investigates a wide variety of biomarkers in the same cohort and correlates them with clinical features and uAD, is one of its main merits. All tests were completed in a single visit during the first trimester, at the same time that the nuchal translucency and serum indicators tests for Down syndrome were completed. Another aspect of the current study that is noteworthy is that we exclusively analyzed nulliparous women, although most previous studies have included both nulliparous and multiparous women. As a result of the extremely low likelihood of preeclampsia in this cohort, the practical application of preeclampsia screening in low-risk multiparous women is restricted. For high-risk multiparas (for example, those with a history of preeclampsia), screening may be of low clinical relevance due to the fact that preventive therapy and greater surveillance are suggested in this population. Another essential feature is the incorporation of maternal factors such as maternal age, BMI, and ethnicity into the prediction model, which is an important step. Poon et al31 reported that such characteristics are significant predictors of hypertensive problems during pregnancy in nulliparous women, which is consistent with our findings. A combination of clinical features and blood levels of PAPP-A, PlGF, and Inhibin-A resulted in high diagnostic accuracy, with sensitivity of 75 percent and a false-positive rate of 10 percent, respectively. The results of this study, which included Doppler, showed that the complete model, including Doppler, had theoretically 100 percent sensitivity for the detection of early-onset preeclampsia; however, because of the small number of early-onset cases and the poor accuracy of Doppler alone, these results should be interpreted with caution. It has been postulated that an ideal predictive test for preeclampsia would have a very high positive likelihood ratio and a very low negative likelihood ratio (LR 0.1.32), respectively. The majority of positive LR in the current study are in the range of 3–7. This performance is worse than that of one prior study7, and the next step is to confirm its validity in bigger cohorts before suggesting its use in clinical practice in the future. This strategy also offers the possibility of designing large prospective trials of prevention in women who have been identified as being at high risk. Women at high risk for miscarriage are more likely to benefit from preventive medications such as low-dose aspirin if they begin early in their pregnancy and are treated as soon as possible after finding out they are pregnant. According to our knowledge, there has not been a randomized trial that has investigated such preventative medication in women who were screened as high-risk using a combination of characteristics during the first trimester of pregnancy. Comparing the current study to earlier investigations, the prediction accuracy of PP, ADAM, and free B -hCG were all shown to be inadequate. Nicolaides et al11 discovered that using an ELISA assay with a pair of PP specific monoclonal antibodies in the first trimester, a combination of PP and uAD could provide a 90 percent detection rate of early preeclampsia with a 9 percent false-positive rate, resulting in a 9 percent false-negative rate. More recently, the same group of investigators, employing the same technique and reagents as in the current study, discovered that PP did not significantly improve the prediction of early preeclampsia provided by a combination of maternal factors, uterine artery PI, and PAPP-A when used in conjunction with the other variables. An reason for the discrepancies between the results could be due to the fact that different procedures were applied. Previous findings employed a manual assay and a specific monoclonal antibody, but we used an automated assay and a generic monoclonal antibody. To our knowledge, there is no direct comparison of the two approaches available at this time, and the contradicting reports urge for additional research. The fact that serum levels were not corrected for maternal weight and other relevant clinical variables in earlier trials with PP is another drawback of those investigations. In light of the strong association between maternal weight and prenatal protein (PP) levels, as well as the fact that increased BMI is a strong predictor of subsequent preeclampsia, it is critical to adjust maternal levels for weight or BMI when evaluating this marker for the prediction of preeclampsia. The reasons for the disparity between the results of the first trimester uAD study and the results of prior trials remain a mystery. Many recent

investigations have discovered that women who have subsequent early-onset preeclampsia have significantly elevated PI of the uterine arteries during the first trimester. Although we discovered elevated PI in the affected groups in our investigation, the diagnostic accuracy was poor when compared to earlier studies. 4 highly qualified sonographers and physicians with extensive knowledge in ultrasonography and Doppler were responsible for all measurements. At the outset of the trial, all procedures were standardized, and all measurements were entered on a computerized database, which was then examined for quality assurance purposes. When comparing the current study and other reports, we found that the only technical difference between them was where they took samples from the uterine arteries. In our study, we took samples at the level of the internal cervical os, while in other studies, we took samples at the crossing of external iliac vessels. 19 A striking finding was that the median value of uterine artery PI found in the unaffected group was 1.40 in the current cohort and 1.63 in the previous cohort. Another study using the paracervical approach found mean PI indexes of 1.6-1.8 at 11-13 weeks in an unselected population, whereas the study by Baschat et al, using the same technique as the current study, found a mean PI index of close to 1.40 in unaffected women using the same technique as the current study. Further research, ideally a direct prospective comparison, is required to compare the diagnostic accuracy obtained with different sampling sites of the uterine arteries during the first trimester.

V. CONCLUSION

The current research was hampered by the small number of women who were affected, particularly in the case of early-onset instances, according to the findings. Furthermore, because PlGF levels were only available in half of the sample, which included just four women with early-onset preeclampsia, the study's capacity to examine the prognostic accuracy of this marker, alone or in combination, was severely limited. The researchers discovered modest levels of PlGF in all groups of preeclamptic women, despite this constraint, and the inclusion of PlGF did improve the screening models, despite the fact that none of the comparisons were statistically significant. There is another disadvantage to this study, which is that the mean arterial pressure (MAP) was not measured when the participants were included. Recently, it has been suggested that measuring MAP in the first trimester is an important component of early screening models for preeclampsia in pregnant women. The inclusion of MAP in our models may have improved the screening performance, and this readily available parameter should almost certainly be included in any subsequent screening model for preeclampsia in the future. Several women (2 percent of the cohort) were treated with low-dose aspirin (80 mg daily, starting in the first trimester) for a variety of medical reasons during the study period. The study's major findings, however, were not materially altered by the exclusion of these women. In conclusion, our findings showed the effectiveness of screening for preeclampsia in nulliparous women during the first trimester utilizing a combination of maternal features and blood indicators in the first trimester. Although uAD is not required to achieve excellent sensitivity, the prediction model is particularly accurate at predicting subsequent early or severe preeclampsia, which are associated with the greatest amount of maternal and newborn morbidity. Controlled studies should now be conducted in selected groups of nulliparous women who have been identified as being at risk for preeclampsia in the first trimester to evaluate preventive therapies such as low-dose aspirin.

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